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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,112	11/20/2003	Johannes Bartholomaus	107101-10 - WCG	8885

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EXAMINER	
PERREIRA, MELISSA JEAN	

ART UNIT	PAPER NUMBER
1618	

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06/16/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,112	BARTHOLOMAUS ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7,8,27-29,31,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7,8,27-29,31,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/12/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims and Previous Rejections/Objections Status

1. The examiner would like to clarify that the office action mailed 11/18/09 was incorrectly designated as a final rejection. This error has been rectified and the office action mailed 11/18/09 has been correctly designated as a non-final rejection.

2. Claims 1,2,4,7,8,27-29,31,41 and 42 are pending in the application. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

Affidavit/Declaration

3. The declarations of Johannes Bartholomaus, Heinrich Kugelmann and Elisabeth Arkenau-Maric filed on 5/18/10 under 37 CFR 1.131 are sufficient to overcome the Dow Technical Data Polyox reference.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1,2,4,7,8,27-29,31,41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oshlack et al. (US 2003/0064099A1) in view of Zhang et al.

(*Pharm. Dev. Tech.* **1999**, *4*, 241-250) and in further view of Kumar et al. (US 6,238,697B1) and DeJong (*Pharmaceutisch Weekblad Scientific Edition* **1987**, p24-28).

6. Oshlack et al. (US 2003/0064099A1) discloses the preparation of a solid dosage form with reduced abuse potential via a melt-extrusion technique. The solid dosage form comprises a.) oxymorphone (derivatives) including enantiomers, diastereomers, etc. b.) an aversive agent/gelling agent, such as polyethylene oxide, c.) carnauba wax, d.) sustained-release material, etc. (p2, [0026]; p8, [0097]; p9, [0106-0111],[0113-0114]; p4-5 [0049] and [0056]; p16, [0186]). The sustained release oral formulations of the disclosure can be formulated in any suitable tablet, coated tablet or multiparticulate formulation know to those skilled in the art (Oshlack et al. p7, [0081]).

7. The melt-extrusion technique of the disclosure involves blending the opioid with at least one aversive agent, together with a sustained release material to form a homogeneous mixture. The homogeneous mixture is heated to a temperature sufficient to at least soften the mixture, extruding through a twin-screw extruder which consists of two-counter-rotating intermeshing screws and then forcing the homogeneous mixture through a die to form strands where forcing provides for some compaction (p8, [0096-0097]; p9, [0109],[0111]; p10, [0113-0114]; claim 22). The extrudate is preferably cooled and cut/pelletized into multiparticles or compressed/molded into an oral tablet by conventional tableting equipment and standard techniques (p10; [0113], [0117] and [0120]; p11, [0126]). The extrudate provides sustained release of the opioid analgesic for a time period of at least about 12 hours wherein the sustained-release profile of the

melt-extruded formulations of the invention can be altered by varying the amount of sustained-release material, etc. (p3, [0034]; p10, [0113] and [0124]).

8. The melt-extrusion technique of Oshlack et al. encompasses the heating technique of the instant claims which involves mixing the components and optionally after granulation, press-forming with preceding, simultaneous or subsequent exposure to heat.

9. Oshlack et al. does not explicitly disclose the PEO polymer of 1-15 million as the sustained release material or that the dosage form has a breaking strength of at least 500N.

10. Zhang et al. (*Pharm. Dev. Tech.* **1999**, *4*, 241-250) discloses the preparation of stabilized sustained release tablets prepared by hot-melt extrusion. The sustained release tablets prepared by hot-melt extrusion comprise polyethylene oxide (PEO) polymers of molecular weight 1,000,000 and 7,000,000 in the matrix tablet as PEO was shown to be a suitable polymeric drug carrier for this process (abstract; p242, paragraphs 4 and 5; p249, paragraph 1). During the hot-melt extrusion process, a dry powder blend of drug, polymer and other adjuvants were fed into the extruder and melted inside the barrel of the machine, the molten mass was extruded through a rod-shaped die and then cut manually into tablets (abstract; p242, all of the left column; p243, Results and Discussion). The melting point of the polymer ranges from 60 to 75°C (p243, right column first paragraph).

11. Kumar et al. (US 6,238,697B1) discloses extended release dosage form which comprise high molecular weight polyethylene oxide binder (to bind the powder particles

together), in an amount of from about 10 to about 20 percent by weight, to provide for a hard, chip-resistant tablet wherein the polyethylene oxide allows for the slow diffusion of an active agent (abstract; column 3, lines 46-50; column 7, lines 19-28; column 8, lines 54-60). The molecular weight of the polyethylene oxide is most preferably about 5,000,000 and can be varied depending on the dosage size and desired rate of release (column 9, lines 1-27; column 10, lines 1-5).

12. DeJong (*Pharmaceutisch Weekblad Scientific Edition* **1987**, p24-28) discloses the calculation for determining crushing strength wherein the comparison of specific crushing strength with other tablet dimensions can be determined. The specific crushing strength is, of course, a function of the porosity and can be correlated to the porosity by $\tau = \tau_0(1-\epsilon)^m$ in which τ_0 is dependent on the composition and the granulation process and m is an experimental value. The measured crushing strength of the tablet is also a function of the weight of the tablet (p24-25, specific crushing strength). The disclosure shows relationships between specific crushing strength, porosity, friability and disintegration time, than can be described in simple mathematical form. If these properties are known for compacted tablets of a certain porosity, the crushing strength, friability and disintegration time at other porosities can easily be predicted (p27, conclusion).

13. At the time of the invention it would have been obvious to one skilled in the art to use the PEO of high molecular weight of Zhang et al. for the sustained release dosage forms of Oshlack et al. as the disclosures are drawn to the same utility, such as sustained release dosage forms having sustained release material, such as PEO of

Zhang et al. which are used for the preparation of melt-extruded tablets via a melt-extrusion technique, which encompasses the sintering technique of the instant claims which recites press-forming with preceding exposure to heat.

14. At the time of the invention it would have been obvious to one skilled in the art that the sustained release dosage forms of the combined references of Oshlack et al. and Zhang et al. contains a high molecular weight PEO polymer in an amount sufficient to result in a breaking strength of at least 500N as Kumar et al. teaches that tablets comprising high molecular weight PEO binders from about 10 to about 20 percent by weight to provide for a hard, chip-resistant tablet and DeJong teaches shows the relationships between specific crushing strength, porosity, friability and disintegration time, than can be described in simple mathematical form.

15. In regards to the amount of PEO, such as of at least 30 wt%, it is obvious to vary and/or optimize the amount of (compound) provided in the composition, according to the guidance provided by (reference), to provide a composition having the desired properties such as the desired (ratios, concentrations, percentages, etc.) as Oshlack et al. teaches that melt-extruded formulations of the invention can be altered by varying the amount of sustained-release material, etc. to provide for the sustained release of the drug over at least 12 hours and Kumar et al. teaches that PEO may be included in a dosage form in an amount of from about 10 to about 20 percent by weight but be varied depending on the dosage size and desired rate of release. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover

the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

16. It is respectfully pointed out that instant claim 29 is a product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Response to Arguments

17. Applicant's arguments with respect to claims 1,2,4,7,8,27-29,31,41 and 42 have been considered but are moot in view of the new ground(s) of rejection.

18. Applicant's assertions of Oshlack's teaching of PEO as a gelling agent is moot in view of the new grounds of rejection.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618